REMARKS

Applicants previously filed a Request for Continued Examination ("RCE") on July 8, 2004, with an Amendment. The Examiner ruled that the RCE was non-responsive as being directed to non-elected claims in accordance with MPEP § 821.03. Applicants therefore submit this revised Amendment. Claims 1-64 are cancelled, with claims 1-39 being previously cancelled and claims 40-64 cancelled herein. New claims 65-93 are added to replace the cancelled claims. New claims 65-93 are supported by the original claims and specification.

As noted in the specification, the present invention relates to increasing the bioavailability of a lipophilic bioactive compound by the novel feature of associating the lipophilic bioactive compound with a whey protein to form a mixture (*see, e.g.*, specification, p. 8, line 19 to p. 10, line 11 (providing that the present composition is formed as a mixture of a lipophilic bioactive compound and whey protein); p. 5, lines 21-24; p. 7, lines 1-4; and p. 8, lines 12-18 (disclosing the benefits of the present composition of increasing the bioavailability of a lipophilic bioactive compound)). The new claims emphasize this inventive and advantageous feature of the present application. The title is also amended to reflect the new claims. As no new matter has been introduced, Applicants respectfully request that the new claims be entered in the application at this time.

Claim Rejections -- 35 U.S.C. § 102

The Examiner rejects claims 1-8, 10-16, 18-21 and 32-39 under § 102(b) as being anticipated by Potter *et al.* (U.S. Patent No. 5,855,892 A). Potter relates to a method of altering the concentration of cholesterol constituents in human blood by administering a daidzein material. The daidzein material may be administered in a pharmaceutical composition or in a dietary supplement, including soy protein-based dietary supplements. Potter discloses that daidzein is isolated from a soy material, including soy beans, dehulled soy beans, soy meal, soy flour, soy grits, soy flakes (full fat and defatted), soy molasses, soy protein concentrates, soy whey, soy whey protein, and soy protein isolate (col. 3, line 60 to col. 4, line 16), and that a daidzein-rich soy protein material can be formed by producing a protein isolate from defatted soy flake such that the loss of daidzein from the protein isolate is

minimized or by converting daidzin and daidzein isoflavone conjugates to daidzein in a soy protein concentrate or in a soy whey protein material (col. 6, lines 31-63).

Thus, Potter, which teaches a composition comprising daidzein and a soy whey protein material, it makes no mention of whey protein. Although the inclusion of the word "whey" in "soy whey protein" may appear misleading, a person skilled in the art would immediately understand that a "soy whey protein" is a soy protein concentrate or isolate, and not a whey protein that is used in the present invention.

In this respect, Applicants would like to stress that whey protein, which as noted above is a milk byproduct and of dairy origin, and soy protein (or "soy whey protein" as called in Potter) are distinctly different types of protein. While the specification does not explicitly provide that the whey protein is derived from milk, Applicants would like to point out that the term "whey protein" is generally understood, not only in the art but also in the public, as identifying a protein of dairy origin, and respectfully submit that a person skilled in the art would readily understand the difference between "whey protein" as used in the present application and the "soy whey protein" of Potter.

Therefore, Potter does not teach, disclose or suggest combining daidzein with whey protein, an important and novel feature of the present invention that enables increased bioavailability.

Moreover, the present compositions significantly differ from the Potter composition in that the lipophilic bioactive compound in Potter is isolated from soy and is provided in a soy-based material, rather than being added exogenously as in the present invention (*see, e.g.,* p. 8, lines 19-30 of the specification, which shows that the LBC is separately and exogenously added in the present composition, as opposed to being isolated from the whey protein material).

The ratio of daidzein to soy protein by weight further emphasizes the difference between the Potter composition and the present invention. As stated for Formulations 5-8 in Potter, which illustrate dietary supplements that may be formed using an isolated soy protein rich in daidzein, the daidzein-rich isolated soy protein typically contains between about 1 to 3 milligrams of daidzein per gram of soy protein. The weight ratio of daidzein to soy protein in Potter is thus 1:1,000 to 3:1,000, far from that of LBC to whey protein in the present invention, and certainly not an amount effective to increase the bioavailability of the LBC. In contrast, the present invention discloses that "the whey protein and lipophilic bioactive

compound may be present in a weight ratio of at least about 1:1 to 500:1, preferably from about 1.5:1 to 250:1 and more preferably about 2:1 to 20:1" (specification, page 6, lines 14-18).

Thus, the Examiner's statement that the amount of the materials in Potter "would certainly comprise the claimed amounts of 0.05-50% LBC and 5-90% whey protein, as well as the 1:1 ratio as claimed by applicant" (p. 5, Office Action) is incorrect. In Formulations 5-8 in Potter, for example, the weight ratio of daidzein to soy protein would be 1:1,000 to 3:1,000, given that the daidzein-rich isolated soy protein typically contains between about 1 to 3 milligrams of daidzein per gram of soy protein and that no additional daidzein is exogenously added. The LBC in the Potter composition is therefore present in an amount far less than 0.05-50% of the composition.

Accordingly, the present invention is not anticipated by Potter, which makes no mention of bioavailability enhancement of the LBC, isolates daidzein from soy protein instead of adding exogenously, and uses a weight ratio of components that is so far removed from the present invention that it does not inherently disclose increasing the bioavailability of a lipophilic bioactive compound. The claim rejection over Potter should therefore be withdrawn.

The Examiner also rejects claims 1-10, 13-14, 16, and 18-21 under § 102(b) as being anticipated by Schmitz *et al.* (U.S. Patent No. 5,643,623 A). Schmitz teaches a health food product containing a first component in the form of a discrete portion from a second component. The first component includes an antioxidant mixture containing a blend of antioxidants selected from carotenoids, vitamins C and E, and curcumin. Internalization and integration of the above nutrients within a lipid-containing core of the food product facilitates absorption of the fat-soluble components in the gastrointestinal tract following consumption, increases shelf-life and minimizes degradation of these labile compounds by minimizing exposure to heat, light and/or oxygen, and prevents disadvantageous yellow/orange coloration of the outer material of the food product.

The Examiner states that Schmitz teaches food product compositions comprising lycopene, vitamins C and E, whey protein, flavors, and colors in the form of solid, gel or liquid, citing Example 6, which discloses that whey protein may be included as carrier in the first or second component. As shown in the example, the first component contains 10-20% of whey protein which is used as carrier in the lipid-containing core and 0.1-1% carotenoid

blend (the lipophilic compound). The second component contains only carrier compounds and no LBC, as specified in the description ("The second component comprises a carbohydrate and/or fat and/or protein, and advantageously other nutritive and non-nutritive compounds" (col. 2, line 66 to col. 3, line 1)). Hence, the Schmitz composition is in an encapsulated form and therefore is heterogeneous, contrary to the present invention, wherein the composition is a homogenous mixture. Rather than being in a discrete form as in Schmitz, the LBC is distributed uniformly throughout the protein component in the present invention, thereby providing the unexpected and important benefit of increased bioavailability of the LBC. It should also be noted that Schmitz urges one skilled in the art to use a lipid-containing core and does not teach that the lipid core may be replaced by whey protein as a matrix.

In addition to teaching the inclusion of an antioxidant mixture in a food product only in an encapsulated form, Schmitz does not disclose, teach or suggest enhancing bioavailability of the carotenoid blend, but only contemplates using whey protein as a carrier. Schmitz specifies that the antioxidants are preferably localized in a lipid-based carrier within the food product to promote absorption and digestion of the carotenoid blend and curcumin (col. 3, lines 19-22). Whey protein is cited in Schmitz only as an example of different kinds of proteins that can be used as carrier, and its important function related to bioavailability is not recognized.

Further, the claims have been amended to recite that the present compositions are homogeneous and are provided in an unencapsulated form, as a mixture of whey protein and an LBC. As previously noted, the support for the unencapsulated, mixture form of the composition is found in the present specification, specifically at p. 8, line 19 to p. 10, line 11 (*see, e.g.*, p. 8, lines 19-22 (providing that in the process "for the preparation of the primary composition . . . the whey protein is mixed with the lipophilic bioactive compound"). Because of this significant difference in form with respect to how whey protein and LBC are provided, Schmitz, relating only to an encapsulated form, does not inherently disclose the function of the present composition (i.e., the function of increasing the bioavailability of the LBC by providing the LBC in a mixture with whey protein), and the Examiner's statement that "such as function is inherent to the composition of Schmitz" (p. 8, Office Action) is incorrect.

Accordingly, Applicants respectfully request that the claim rejection be withdrawn.

Claims 1-7, 9-10 and 20-21 are rejected under 35 U.S.C. §§ 102(a) and 102(e) as being anticipated by Collins *et al.* (U.S. Patent No. 6,203,805 B1). Collins relates to pharmaceutical or cosmetic compositions for topical application to the skin comprising a collagen enhancing effective amounts of whey protein, vitamin A, vitamin E and vitamin C in combination with each other.

Collins teaches a synergistic combination that enhances the stimulation of collagen synthesis, for which there had previously been a research involving a peptide in the form of a hydrolysate, obtained from fermentation of milk proteins. Specifically, Collins discloses that when vitamins C and E are combined in specific ranges of amounts with whey protein and vitamin A, an inverse relationship is found between quantities specific to vitamin C and vitamin E with respect to increasing the production of collagen. Collagen production is maximized using higher quantities specific to vitamin E and lower quantities specific to vitamin C and, conversely, using lower quantities specific to vitamin E and higher quantities specific to vitamin C, within certain defined ranges. For example, while whey protein alone increased collagen synthesis by 85 percent, the composition was shown to be capable of boosting the synthesis of collagen greater than about 300 percent when vitamins C and E components were present in specific ranges. However, there was a decrease in collagen synthesis when vitamin C is doubled (from 50 μg/ml to 100 μg/ml) in the presence of a high level of vitamin E (1,000 μg/ml).

Thus, what Collins teaches is that collagen synthesis can be enhanced by using whey protein and vitamin A, in combination with vitamins C and E in specific ranges based on their inverse effect in boosting collagen synthesis. The vitamins enhance the collagen-stimulating property of whey protein, but only if they are used in certain limited amounts in relation to each other. Hence, the Collins composition does not teach how whey protein can enhance the bioavailability of an LBC, and a skilled artisan would not consider the present invention to be anticipated by a disclosure that relates to how certain vitamins in certain amounts can boost the collagen-stimulating ability of whey protein.

In addition, as the Examiner points out, the whey protein is present in the Collins composition in the amounts of 50-10,000 μg/ml, which correspond to 0.005-1% by weight. Such is not an amount that is effective to increase the bioavailability of the LBC. In the present invention, whey protein represents at least 5% and up to 90% of the composition to enhance the bioavailability of the LBC (specification, page 6, lines 13-14).

Hence, the Examiner's statement that "[the function of enhancing the bioavailability of the LBC] is inherent to the composition of Collins" (p. 9, Office Action) is incorrect. As the previous explanation shows, it is critical that specific ingredients are provided in specific amounts in Collins based on the inverse relationship between the amounts of certain vitamins and collagen production. Therefore, Collins neither teaches nor discloses nor suggests, whether directly or inherently, enhancing the LBC bioavailability by mixing whey protein and the LBC. Mixing an LBC with whey protein to enhance the LBC bioavailability is not inherent in the Collins composition, and the amounts of each ingredient used in the Collins composition further evince this difference.

Accordingly, Applicants respectfully request the rejection based on Collins be withdrawn.

Claims 1-7, 11-14, 18-21, 32-33 and 36 are rejected under § 102(b) as being anticipated by Rosenberg (U.S. Patent No. 5,601,760), which describes a milk derived whey protein-based microencapsulating agents and a method for microencapsulation of volatile or non-volatile core materials in a wall system consisting essentially of a whey protein. Whey protein-microencapsulated cores are disclosed as being easy to handle and store, having higher stability, protecting the encapsulated core from deteriorating factors, preventing evaporation of volatile cores, transforming liquid cores into free flowing powders, and providing greater versatility of microencapsulated products.

The term "core" is used to mean any active ingredient or material submitted to microencapsulation by whey proteins, with examples including fats such as anhydrous milk fat, volatiles, essential oils, flavors, fragrances, nutritional compounds, health products, vitamins, oleoresins, bacteria, enzyme, minerals, natural colorants, oils, essences, pharmaceuticals, and pharmaceutically acceptable ingredient, or a mixture thereof. The concentration (load) of cores used for microencapsulation depends on the active ingredient and typically ranges from about 5% to 95% by weight of the dry wall solids. The wall system of the Rosenberg invention is formed by milk derived whey protein isolate or whey protein concentrates alone or in combination with milk derived or non-milk derived carbohydrates.

In Example 6, Rosenberg teaches a composition that contains a certain amount of whey protein in the wall system and a certain amount of molecules to be encapsulated in the core, which is, more specifically, a composition comprising 35-80% whey protein and 10-75% vitamin A. Similar to the Schmitz composition, the composition in Rosenberg is in an

encapsulated form and is heterogeneous, unlike the present invention, in which the composition is a homogeneous mixture. Instead of being in discrete encapsulated forms, the LBC is distributed uniformly throughout the whey protein component to form a mixture in the present invention.

Because Rosenberg seeks to utilize the suitability of whey protein as a microencapsulating agent based on its stability, safety for consumption, and ease of handling and storage, Rosenberg uses whey protein in a manner that is completely different from that of the present claims. Specifically, rather than being mixed with an LBC in a mixture, the whey protein in Rosenberg encapsulates a core material, completely coating the core material such that it is shielded from light, air and physical contact. In contrast to the prior art, the whey protein according to the present claims does not cover or embed an LBC but is mixed with it such that the bioavailability of the LBC is enhanced. Hence, because Rosenberg does not disclose, teach or suggest enhancing bioavailability of core materials with whey protein, but merely teaches using whey protein as a microencapsulating agent for easy handling and storage of core materials, Rosenberg does not anticipate the present composition.

Applicants also note that Rosenberg does not provide a clear and sufficient disclosure with respect to the amounts to be used. For instance, Example 6 only provides: "Vitamin A was emulsified in whey protein concentrates having 35-80% protein or in whey protein concentrate. Wall solids concentrations were from 10-40% (w/w). Core of vitamin A to wall solids ratio was from 10-75%." The Examiner reads this to mean "a composition comprising 10-75% vitamin A and 35-80% whey protein," which naturally cannot be an "intimate" mixture like the present invention.

In contrast, the present invention is directed to increasing the bioavailability of the LBC by providing a mixture of whey protein and LBC, and therefore to an invention different from Rosenberg, as amended claims emphasize. Accordingly, Applicants respectfully submit that the present invention is not anticipated or rendered obvious to the skilled artisan familiar with Rosenberg and that the claim rejection based on Rosenberg should also be withdrawn.

Claim Rejections -- 35 U.S.C. § 103

Claims 1-16, 18-21 and 32-39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Potter and Fujiwara. Potter teaches pharmaceutical/supplemental compositions comprising daidzein, soy whey protein, and vitamins that can be effective in

decreasing LDL and increasing HDL. Fujiwara teaches a pharmaceutical composition comprising lycopene, soybean oil, and vitamin E, and also teaches that the composition is effective in decreasing LDL and increasing HDL. Although the references do not teach a composition comprising lycopene, soy extract and whey protein, the Examiner concludes that the invention as a whole is *prima facie* obvious over the references, because it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the instant ingredients since each is well known to decrease LDL and increase HDL.

It appears, however, that the Examiner is making an *ex post facto* analysis with little relevance to the present invention. Lipophilic bioactive compounds are known in the art to be used in food or pharmaceutical compositions, but they are very often not bioavailable, particularly in the case of lycopene. The aim of the present invention is to increase bioavailability of the LBC, and the inventive step of the present application is not made obvious by Potter and Fujiwara, either alone or in combination. In fact, a skilled artisan trying to solve the problem of bioavailability of the LBC is unlikely to look into Potter and Fujiwara, as these references do not even discuss whey protein and bioavailability.

Thus, contrary to the Examiner's statement on page 15 of the Office Action, one or ordinary skill in the art would not have been motivated to combine the instant ingredients to achieve increased LBC bioavailability merely based on the fact that each ingredient is known to decrease LDL and increase HDL. Each ingredient's known function of decreasing LDL and increasing HDL is simply irrelevant to, and does not render obvious, the function of increasing the LBC bioavailability which is achieved by providing the LBC and whey protein in a mixture form in the present application.

Accordingly, this claim rejection is inappropriate and should be withdrawn.

The Examiner also rejects claims 1-16, 18-21 and 32-39 under § 103(a) as being unpatentable over Schmitz, which teaches food product compositions comprising lycopene, vitamins C and E, whey protein, flavors and colors, in the form of solid, gel or liquid. While Schmitz does not teach the composition comprising specific amounts and ratios of LBC and whey protein, or wherein the composition is in the claimed food forms, the Examiner states that it would have been well within the purview of one of ordinary skill in the art to optimize such amounts and forms as a matter of routine experimentation. The Examiner further states that, at the time of the claimed invention, one of ordinary skill in the art would have been

motivated by routine practice to optimize the various parameters of the Schmitz composition with a reasonable expectation for successfully obtaining a food product.

As stated above, however, the Schmitz composition is in an encapsulated form and therefore is heterogeneous, whereas the composition of the present invention is a homogenous mixture. In contrast to the Schmitz composition, the LBC and the whey protein are distributed throughout the entire composition and uniformly with each other in the present invention, as emphasized in the amended claims. One of ordinary skill in the art would only know to use a lipid-containing core under Schmitz, as it specifies that the antioxidants are preferably localized in a lipid-based carrier within the food product to promote absorption and digestion of the carotenoid blend and does not disclose, teach or suggest that the lipid core may be eliminated and replaced with whey protein as a mixture. Schmitz, moreover, does not provide any information about enhancing bioavailability of the carotenoid blend, but contemplates using whey protein merely as carrier.

Because the Schmitz composition is presented in a form that is completely different from, and is not interchangeable with, that of the present invention and makes no mention or suggestion of enhancing bioavailability, one of ordinary skill in the art would have no motivation to experiment to optimize the parameters of the Schmitz composition to arrive at the presently claimed compositions. Because of the fundamental difference in the nature of the composition between Schmitz and the present invention, it would not have been obvious to a person skilled in the art to experiment with the Schmitz composition in encapsulated form to successfully reach the present composition in mixture form and the resulting benefit of increased LBC bioavailability. Likewise, the function and benefit of the present mixture composition could not have been inherent in the encapsulated Schmitz composition because of their significant differences in form and functional properties.

Therefore, this § 103(a) rejection should also be withdrawn.

Applicants would like to emphasize that, as noted in the specification, the present invention relates to increasing the bioavailability of a lipophilic bioactive compound by the novel feature of associating the lipophilic bioactive compound with a whey protein to form a mixture. By mixing an LBC with a whey protein, the present invention makes available to a subject an LBC-containing composition with better bioavailability compared to consuming an LBC alone (*see, e.g.*, p. 3, lines 6-8; p. 5, lines 11-14). While the prior art references cited in the Office Action may have sought to provide bioactive compounds for health-related

purposes, none of these references has recognized the bioavailability-enhancing function of whey protein that can be utilized by mixing the whey protein with an LBC.

As summarized in Example 1 of the present specification, administration of Applicants' composition -- formed by mixing a lipophilic bioactive compound, such as lycopene, with a whey protein in a mixture form -- has shown that the composition's LBC bioavailability is comparable to that of tomato puree or paste, which is known to have the best bioavailability of lycopene. The data from the study outlined in Example 1 was submitted as Exhibit A in the previous response dated July 8, 2004. For these reasons, Applicants respectfully request that the rejections based on obviousness be withdrawn.

In view of the preceding explanation, it is believed that the entire application is now in condition for allowance, early notification of such would be appreciated. Should the Examiner not agree, a personal or telephonic interview is respectfully requested to discuss any remaining issues in order to expedite the eventual allowance of the claims.

Respectfully submitted,

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